

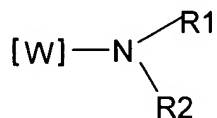
CLAIMS

1. New medicament comprising, in a pharmaceutically acceptable vehicle, an antipsychotic or an antidepressant (A), which, on its own, has an undesirable effect of a gain in body weight or sedation, and an antagonist and/or inverse agonist (B) of the histamine H₃ receptor, the antipsychotic or antidepressant being present in the medicament in a therapeutically effective amount for the antipsychotic or antidepressant effect sought, and the antagonist and/or inverse agonist of the histamine H₃ receptor being present in a therapeutically effective amount for ensuring at least one of the following three effects: suppression or at least limitation of the undesirable effect of weight gain, suppression or limitation of the undesirable effect on alertness, increase in the procognitive effect of the treatment.

2. Medicament according to claim 1, wherein the antipsychotic or antidepressant has an undesirable effect of a gain in body weight and/or sedation due principally to a histamine (H₁) antagonistic effect.

3. Medicament according to either claim 1 or claim 2, wherein the antipsychotic or antidepressant (A) is selected from the group formed by olanzapine, risperidone, clozapine, quetiapine, mirtazapine, paroxetine, amitriptyline, aripiprazole and carbamazepine.

4. Medicament according to any one of claims 1 to 3, wherein the antagonist/inverse agonist (B) of histamine at the H₃ receptor is a compound corresponding to the formula (I)



(I)

in which

W is a residue which, when it is attached to an imidazole ring in the 4 (5)-position, confers on such a molecule an antagonist or inverse agonist activity at the histamine H₃ receptor,

5 R^1 and R^2 , which may be identical or different, each represent, independently,

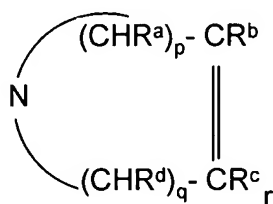
- a C1-C6 alkyl or a cycloalkyl,
- or, taken together with the nitrogen atom to which they are attached,
- a saturated nitrogen-containing ring

10 i)



in which m is from 2 to 8 or
a non-aromatic unsaturated nitrogen-containing ring

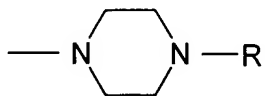
15 ii)



in which p and q independently are from 0 to 3 and r is from 0 to 4, provided that p and q are not simultaneously 0 and that $2 \leq p+q+r \leq 8$,

20 R^{a-d} being, independently, a hydrogen atom or a C1-C6 alkyl group, a cycloalkyl or an alkoxy carbonyl or

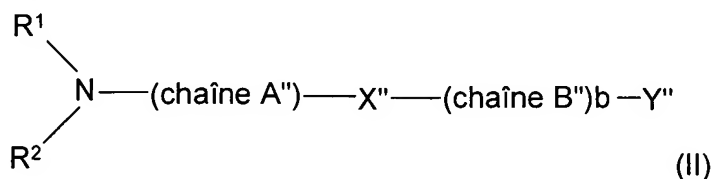
- a morpholino group or
- an N-substituted piperazino group



25 R being a C1-C6 alkyl group, cycloalkyl, alkoxy carbonyl, aryl, arylalkyl, alkanoyl or an aroyl group,

or its pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic crystalline structures of those compounds or their optical isomers, racemates, diastereoisomers or enantiomers.

- 5 5. Medicament according to claim 4, wherein compound (B) corresponds to formula (II)



in which:

b = 0 or 1,

- 10 i) R^1 and R^2 are as defined in formula (I)
- ii) the chain A'' is selected from the linear or branched, saturated or unsaturated hydrocarbon chains containing from 1 to 6 carbon atoms, the saturated hydrocarbon chain optionally being interrupted by a hetero atom which may be a sulphur atom,
- 15 iii) X'' is selected from the oxygen and sulphur atoms, -NH-, -NHCO-, -N(alkyl)CO-, -NHCONH-, -NH-CS-NH-, -NHCS-, -O-CO-, -CO-O-, -OCONH-, -OCON(alkyl)-, -OCON(alkene)-, -OCONH-CO-, -CONH-, -CON(alkyl)-, -SO-, -CO-, -CHOH-, -N(saturated or unsaturated alkyl)-, -S-C(=NY'')-N-Y'', in which the Y''s may be identical or different, and -NR''C(=NR'')-NR'', in which R'' and R''' denote a hydrogen atom or a C1-C6 alkyl radical and R''' denotes a hydrogen atom or another powerful electronegative group which may be selected from a cyano or COY₁'' group, Y₁'' denoting an alkoxy group;
- 20 iv) the chain B'' is selected from an aryl, arylalkyl, arylalkanoyl group; a linear alkylene chain -(CH₂)_n-, n being from 1 to 5, or a branched alkylene chain containing from 2 to 8 carbon atoms, the alkylene chain optionally being interrupted by one or more oxygen or sulphur atoms; and a -(CH₂)_n-O- or -CH₂)_n-S- group in which n is 1 or 2; and
- 25 v) Y'' is selected from a linear or branched alkyl group containing from 1 to 8 carbon atoms; a cycloalkyl containing from 3 to 6 carbon atoms; a bicycloalkyl group; a cycloalkenyl group; an aryl group optionally substituted by a
- 30

phenyl group; a heterocyclic radical having 5 or 6 elements containing one or two hetero atoms selected from nitrogen and sulphur, the heterocyclic radical optionally being substituted; and a bicyclic radical resulting from the fusion of a benzene ring to a heterocycle as defined above;

5 or

ii') the chain A'' is selected from a saturated or unsaturated, linear or branched alkylene group $-(CH_2)_{n''}-$ in which n'' is an integer from 1 to 8; a linear or branched alkenylene group comprising from 1 to 8 carbon atoms; and a linear or branched alkynylene group comprising from 1 to 4 carbon atoms;

10 iii') the group X'' is selected from $-OCONH-$, $OCON(alkyl)-$, $-OCON(alkene)-$, $-OCO-$, $-OCOSNH-$, $-CH_2-$, $-O-$, $-OCH_2CO-$, $-S-$, $-CO-$, $-CS-$, an amine or a saturated or unsaturated alkyl;

iv') the chain B'' is selected from the saturated or unsaturated, linear or branched alkylenes comprising from 1 to 8 carbon atoms; and
15 $-(CH_2)_{n''}(\text{hetero atom})-$ where the hetero atom is preferably an oxygen or sulphur atom; n'' being an integer from 1 to 5; and

v') the group Y'' represents a phenyl group which is unsubstituted or mono- or polysubstituted by one or more identical or different substituents selected from the halogen atoms, OCF_3 , CHO , CF_3 , $SO_2N(alkyl)_2$ such as
20 $SO_2N(CH_3)_2$, NO_2 , $S(aryl)$, $SCH_2(phenyl)$, a linear or branched alkene, a linear or branched alkyne optionally substituted by a trialkylsilyl radical, $-O(alkyl)-$, $-O(aryl)$, $-CH_2CN$, a ketone, an aldehyde, a sulphone, an acetal, an alcohol, a C_1-C_6 alkyl, $-CH=CH-CHO$, $-C(alkyl)=N-OH$, $-C(alkyl)=N-O(alkyl)$ and other ketone derivatives, $-CH=NOH$, $-CH=NO(alkyl)$ and other aldehyde
25 derivatives, $-C(alkyl)=NH-CONH_2$, and O-phenyl or the group $-OCH_2(phenyl)$, $-C(cycloalkyl)=NOH$, $-C(cycloalkyl)=N-O(alkyl)$; an optionally substituted heterocycle, a cycloalkyl; a bicyclic group and preferably a norbornyl group; a phenyl ring fused to a heterocycle comprising a nitrogen hetero atom or to a carbocycle or to a heterocycle having a ketone function; a linear or branched
30 C_1-C_6 alkyl comprising from 1 to 8 carbon atoms; a linear or branched alkyne comprising from 1 to 8 carbon atoms and especially from 1 to 5 carbon atoms; a linear or branched alkyl mono- or polysubstituted by phenyl groups which are

unsubstituted or mono- or polysubstituted; a phenyl alkyl ketone in which the alkyl group is linear or branched or cyclic; a substituted or unsubstituted benzophenone; a substituted or unsubstituted, linear, branched or cyclic phenyl alcohol; a linear or branched alkene; a piperidyl group; a phenyl cycloalkyl group; a polycyclic group, especially a fluorenyl group, a naphthyl or polyhydronaphthyl group or an indanyl group; a phenol group; a ketone or a ketone derivative; a diphenyl group, a phenoxyphenyl group; a benzyloxyphenyl group, -CN, -alkyl, -aryl, -alkylCOalkyl, -COOalkyl, -COalkyl, -COaryl, -COaralkyl, -COcycloalkyl, -OH, -alkyl(OH), -alkyl(Oalkyl), -NHCOalkyl, -NH₂,

or its pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic crystalline structures of those compounds or their optical isomers, racemates, diastereoisomers or enantiomers.

6. Medicament according to either claim 4 or claim 5, wherein the group Y" is a phenyl group substituted by a halogen atom.

7. Medicament according to any one of claims 4 to 6, wherein the compound (B) is 3-(4-chlorophenyl)propyl-3-piperidinopropyl ether (BF2649), or its pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic crystalline structures of those compounds or their optical isomers, racemates, diastereoisomers or enantiomers.

8. Medicament according to any one of claims 1 to 3, characterized in that compound (B) is an imidazole derivative.

9. Medicament according to any one of claims 1 to 8, wherein the proportions of compound (A) with respect to compound (B) are from 5 to 100 mg of compound (B) for 0.5 to 50 mg of compound (A).

10. Medicament according to any one of claims 1 to 9, suitable for oral administration.

11. Medicament according to claim 10 in the form of tablets, capsules, powder or a drinkable preparation.

12. Medicament according to claim 7, in particular in the form of a tablet, capsule or drinkable preparation combining from 5 to 80 mg of compound (BF2649) with from 3 to 20 mg of olanzapine.

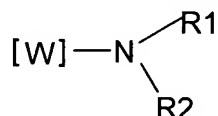
13. Medicament according to claim 7, in particular in the form of a tablet, capsule or drinkable preparation combining from 5 to 80 mg of compound (BF2649) with from 0.5 to 10 mg of risperidone.

14. Medicament according to claim 7, in particular in the form of a tablet, capsule or drinkable preparation combining from 5 to 80 mg of compound (BF2649) with from 10 to 30 mg of aripiprazole.

15. Use of an antagonist and/or inverse agonist of the histamine H₃ receptor (B) for the preparation of a medicament which is to be administered to complement psychiatric treatment by an antipsychotic or an antidepressant in order to prevent or correct the undesirable effects of such a treatment on weight gain and/or alertness which are caused or may be caused by the treatment or in order to potentiate the therapeutic effects of the treatment on the cognitive sphere.

16. Use of an antagonist and/or inverse agonist of the histamine H₃ receptor (B) for the preparation of a medicament which is to be administered to complement psychiatric treatment by an antipsychotic or an antidepressant in order to prevent or correct epilepsy and/or the convulsions which are caused or may be caused by the treatment.

17. Use according to claim 15 or 16, wherein the antagonist/inverse agonist (B) of histamine at the H₃ receptor is a compound corresponding to formula (I)



(I)

in which

W is a residue which, when it is attached to an imidazole ring in the 4 (5)-
position, confers on such a molecule an antagonist or inverse agonist activity at
the histamine H₃ receptor,

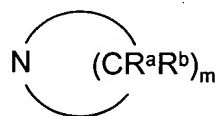
R¹ and R², which may be identical or different, each represent,
independently,

- a C1-C6 alkyl or a cycloalkyl,

or, taken together with the nitrogen atom to which they are attached,

- a saturated nitrogen-containing ring

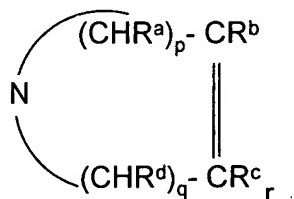
i)



in which m is from 2 to 8 or

a non-aromatic unsaturated nitrogen-containing ring

ii)

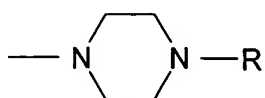


in which p and q independently are from 0 to 3 and r is from 0 to 4, provided
that p and q are not simultaneously 0 and that $2 \leq p+q+r \leq 8$,

R^{a-d} being, independently, a hydrogen atom or a C1-C6 alkyl group, a
cycloalkyl or an alkoxy carbonyl or

- a morpholino group or

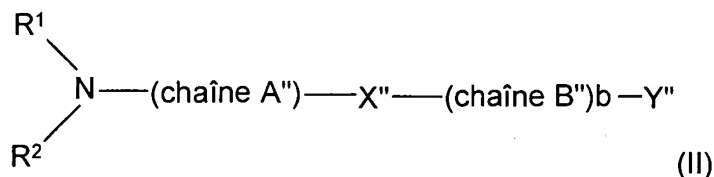
- an N-substituted piperazino group



R being a C1-C6 alkyl group, cycloalkyl, alkoxy carbonyl, aryl, arylalkyl,
alkanoyl or an aroyl group,

or its pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic crystalline structures of those compounds or their optical isomers, racemates, diastereoisomers or enantiomers.

- 5 18. Use according to claim 17, wherein compound (B) corresponds to formula (II)



in which:

b = 0 or 1,

- 10 i) R^1 and R^2 are as defined in formula (I)
- ii) the chain A'' is selected from the linear or branched, saturated or unsaturated hydrocarbon chains containing from 1 to 6 carbon atoms, the saturated hydrocarbon chain optionally being interrupted by a hetero atom which may be a sulphur atom,
- 15 iii) X'' is selected from the oxygen and sulphur atoms, --NH-- , --NHCO-- , --N(alkyl)CO-- , --NHCONH-- , --NH-CS-NH-- , --NHCS-- , --O-CO-- , --CO-O-- , --OCONH-- , --OCON(alkyl)-- , --OCON(alkene)-- , --OCONH-CO-- , --CONH-- , --CON(alkyl)-- , --SO-- , --CO-- , --CHOH-- , $\text{--N(saturated or unsaturated alkyl)--}$, $\text{--S-C(=NY'')--N-Y''--}$, in which the Y''s may be identical or different, and $\text{--NR''C(=NR'')--NR''--}$, in which R'' and R''
- 20 denote a hydrogen atom or a C1-C6 alkyl radical and R'' denotes a hydrogen atom or another powerful electronegative group which may be selected from a cyano or COY_1 group, Y_1 denoting an alkoxy group;
- iv) the chain B'' is selected from an aryl, arylalkyl, arylalkanoyl group; a linear alkylene chain $\text{--(CH}_2\text{)}_n\text{--}$, n being from 1 to 5, or a branched alkylene chain
- 25 containing from 2 to 8 carbon atoms, the alkylene chain optionally being interrupted by one or more oxygen or sulphur atoms; and a $\text{--(CH}_2\text{)}_{n''}\text{--O--}$ or $\text{--(CH}_2\text{)}_{n''}\text{--S--}$ group in which n'' is 1 or 2; and
- v) Y'' is selected from a linear or branched alkyl group containing from 1 to 8 carbon atoms; a cycloalkyl containing from 3 to 6 carbon atoms; a
- 30 bicycloalkyl group; a cycloalkenyl group; an aryl group optionally substituted by a

phenyl group; a heterocyclic radical having 5 or 6 elements containing one or two hetero atoms selected from nitrogen and sulphur, the heterocyclic radical optionally being substituted; and a bicyclic radical resulting from the fusion of a benzene ring to a heterocycle as defined above;

5 or

ii') the chain A'' is selected from a saturated or unsaturated, linear or branched alkylene group $-(CH_2)_{n''}-$ in which n'' is an integer from 1 to 8; a linear or branched alkenylene group comprising from 1 to 8 carbon atoms; and a linear or branched alkynylene group comprising from 1 to 4 carbon atoms;

10 iii') the group X'' is selected from $-OCONH-$, $OCON(alkyl)-$, $-OCON(alkene)-$, $-OCO-$, $-OCOSNH-$, $-CH_2-$, $-O-$, $-OCH_2CO-$, $-S-$, $-CO-$, $-CS-$, an amine or a saturated or unsaturated alkyl;

iv') the chain B'' is selected from the saturated or unsaturated, linear or branched C2-C6 alkenes comprising from 1 to 8 carbon atoms; and
15 $-(CH_2)_{n''}(\text{hetero atom})-$ where the hetero atom is preferably an oxygen or sulphur atom; n'' being an integer from 1 to 5; and

v') the group Y'' represents a phenyl group which is unsubstituted or mono- or polysubstituted by one or more identical or different substituents selected from the halogen atoms, OCF_3 , CHO , CF_3 , $SO_2N(alkyl)_2$ such as
20 $SO_2N(CH_3)_2$, NO_2 , $S(aryl)$, $SCH_2(phenyl)$, a linear or branched alkene, a linear or branched alkyne optionally substituted by a trialkylsilyl radical, $-O(alkyl)-$, $-O(aryl)$, $-CH_2CN$, a ketone, an aldehyde, a sulphone, an acetal, an alcohol, a C₁-C₆ alkyl, $-CH=CH-CHO$, $-C(alkyl)=N-OH$, $-C(alkyl)=N-O(alkyl)$ and other ketone derivatives, $-CH=NOH$, $-CH=NO(alkyl)$ and other aldehyde
25 derivatives, $-C(alkyl)=NH-CONH_2$, and O-phenyl or the group $-OCH_2(phenyl)$, $-C(cycloalkyl)=NOH$, $-C(cycloalkyl)=N-O(alkyl)$; an optionally substituted heterocycle, a cycloalkyl; a bicyclic group and preferably a norbornyl group; a phenyl ring fused to a heterocycle comprising a nitrogen hetero atom or to a carbocycle or to a heterocycle having a ketone function; a linear or branched
30 alkyl comprising from 1 to 8 carbon atoms; a linear or branched alkyne comprising from 1 to 8 carbon atoms and especially from 1 to 5 carbon atoms; a linear or branched alkyl mono- or polysubstituted by phenyl groups which are unsubstituted

- or mono- or polysubstituted; a phenyl alkyl ketone in which the alkyl group is linear or branched or cyclic; a substituted or unsubstituted benzophenone; a substituted or unsubstituted, linear, branched or cyclic phenyl alcohol; a linear or branched alkene; a piperidyl group; a phenyl cycloalkyl group; a polycyclic group, especially
- 5 a fluorenyl group, a naphthyl or polyhydronaphthyl group or an indanyl group; a phenol group; a ketone or a ketone derivative; a diphenyl group, a phenoxyphenyl group; a benzyloxyphenyl group, -CN, -alkyl, -aryl, -alkylCOalkyl, -COOalkyl, -COalkyl, -COaryl, -COaralkyl, -COcycloalkyl, -OH, -alkyl(OH), -alkyl(Oalkyl), -NHCOalkyl, -NH₂,
- 10 or its pharmaceutically acceptable salts, hydrates, or hydrated salts, or the polymorphic crystalline structures of those compounds or their optical isomers, racemates, diastereoisomers or enantiomers.
- 15 19. Use according to either claim 17 or claim 18, wherein the group Y'' is a phenyl group substituted by a halogen atom.
- 20 20. Use according to claim 15 or 16, wherein the antagonist or inverse agonist is an imidazole derivative.
- 25 21. Use according to any one of claims 15 to 20, wherein the H₃ antagonist/inverse agonist is presented in a form for oral administration, such as a tablet, capsule or drinkable solution, and is to be administered to complement treatment by an antipsychotic or antidepressant, in order to correct the undesirable effects of those drugs.
22. Use according to claim 21 such that the undesirable effects include weight gain, loss of alertness.
- 30 23. Use according to claim 21 such that the undesirable effects include epilepsy and/or convulsions.
24. Use according to any one of claims 15 to 23, wherein the H₃ antagonist/inverse agonist is presented in a form for oral administration, such as a

tablet, capsule or drinkable solution, and is to be administered to complement treatment by an antipsychotic or an antidepressant, in order to potentiate the therapeutic effect thereof on the cognitive sphere.

5 25. Use according to any one of claims 15 to 24, wherein the antipsychotic or an antidepressant is selected from olanzapine, risperidone, clozapine, quetiapine, mirtazapine, paroxetine, amitriptyline, aripiprazole and carbamazepine.

10 26. Use of a compound (A) and a compound (B) as defined according to any one of the preceding claims for the preparation of a medicament for preventing and/or treating a pathology selected from: schizophrenia, depression, psychosis, mental disorders, mania, bipolar affective disorders.